REMARKS

1. Introductory remarks

Claims 1-9 were pending before the Office. By this Amendment, Applicants respectfully request that claims 1-9 be cancelled, without prejudice and new claims 10-29 be added. No claims are amended.

The amendments have been made solely to claim more fully the invention and/or to expedite prosecution of the present application and should in no way be construed as an acquiescence to any of the Examiner's rejections in the Office action issued in the present application. Applicants reserve the right to pursue the subject matter of the claims as originally filed or similar claims in one or more subsequent applications.

Support for the amendments can be found throughout application, including the specification, drawings, examples and claims, as originally filed.

Accordingly, no new matter has been added by this amendment.

Reconsideration and withdrawal of the objections to and the rejections of this application in view of the amendments and remarks herewith, are respectfully requested.

2. The Claims Objections Are Overcome

The Examiner objected to claims 2, 4 and 9 as allegedly being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicants have cancelled claims 1-9 and have added in their place claims 10-29. Accordingly, the present objections are moot.

Applicants do not believe that the objections apply to the new claims 10-29.

Reconsideration and withdrawal of these objections are respectfully requested.

3. The Rejection Under 35 U.S.C. 112, Second Paragraph, Is Overcome

The Examiner rejected claims 1-9 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicants regards as the invention. The alleged basis for the rejection included that the claims lacked any active method steps, lacked sufficient antecedent basis for various limitations (specifically, "the molecule," "the fluorescent lifetime," and "the modified molecule" of claim

1), and lacked sufficient clarity as to the relation of certain limitations (e.g., "enzymes") and the active method steps of the based claims.

Applicants have cancelled claims 1-9 and have added in their place claims 10-29. Accordingly, the present rejections are moot.

Applicants do not believe that the rejections apply to the new claims 10-29 because none of the rationales above for indefiniteness would appear applicable to the new claims.

Reconsideration and withdrawal of the rejection of claims 1-9 are respectfully requested.

4. The Rejection Under 35 U.S.C. 102(b) Is Overcome

The Office Action rejects claims 1-7 and 9 under 35 U.S.C. §102(b) as allegedly being anticipated by Kask (U.S. Published Appl. No. 2002/0063863, now U.S. Patent No. 6,690,463) (hereafter "Kask").

As an initial matter, claims 1-7 and 9 have been cancelled. Thus, the rejection is moot as to those claims. To the extent that the Examiner believes the rejection may apply to new claims 10-29, Applicants respectfully would disagree and traverse as follows.

The Examiner is respectfully pointed to M.P.E.P § 2131 which states that "[a] claim is anticipated ***only if each and every element*** as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *See Verdegaal Bros. V. Union Oil Co. of California*, 814 F.2d 628, 631 (Fed. Cir. 1987) (emphasis added). It will be shown below that Kask does not expressly or inherently teach each and every element of the claimed invention, and thus, does not anticipate the present claims.

The present invention is directed to a method for detecting when a fluorescently-labeled molecule becomes modified from one state to another by a modifying agent using fluorescence lifetime measurements. Claim 10 assumes at the start that the modifying agent can modify the molecule of interest from one state to another, and the focus is on the detection of the modification itself. Claim 20 is aimed at screening for a candidate modifying agent that is capable of modifying a molecule of interest from one state to another.

More in particular, claim 10 recites a method for detecting a modification to a molecule that involves (a) ***measuring*** the fluorescence lifetime of the fluorescently labeled molecule when it is in a first state; (b) ***contacting*** the molecule with a modifying agent that is capable of

changing the molecule from said first state to a second state; and (c) ***measuring*** the fluorescence lifetime of the fluorescently labeled molecule after contacting with the modifying agent, wherein a difference in the fluorescence lifetimes measured in (a) and (c) indicates a modification to the molecule.

Dependent claims 11-19 further define the fluorescent dyes and how they are coupled to the molecule (claims 11-13), the modifying agents (claims 14-16), and the types of molecular modifications or molecular states (claims 17-18). Claim 19 recites that the method provides high-throughput screening of the molecules or modifying agents.

Claim 20 recites a method of screening for a modifying agent that is capable of modifying a molecule in a first state to a molecule in a second state, wherein the molecule is fluorescently labeled and has a different fluorescent lifetime in a first state as compared to a second state. The method comprises (a) ***measuring*** the fluorescence lifetime of the fluorescently-labeled molecule in the first state, (b) ***contacting*** the fluorescently-labeled molecule in the first state with a candidate modifying agent, (c) ***measuring*** the fluorescence lifetime of the fluorescently-labeled molecule after it has been contaced with the candidate modifying agent, and (d) ***comparing*** the fluorescence lifetimes measured in step (a) and step (c), wherein the candidate modifying agent is identified as a modifying agent where there exists a difference in the fluorescent lifetimes.

Dependent claims 21-29 further define the fluorescent labels and how they are coupled to the molecule (claims 21-23), the modifying agents (claims 24-26), and the types of molecular modifications or molecular states (claims 27-28). Claim 29 recites that the method provides high-throughput screening of the molecules or modifying agents.

Thus, the method of the invention concerns the detection of physical modifications to or changes directly to a molecule of interest which are the result of the action or activity of a modifying agent. In a similar aspect, the invention also pertains to the screening for modifying agents that are capable of bringing about or causing such physical changes or modifications to molecules of interest. The molecules of interest are fluorescently-labeled, which allows the detection of physical changes to the molecules themselves using fluorescence lifetime measurements. These features are distinct from and not anticipated by Kask.

Kask relates instead to the detection of ***protein-protein binding interactiosn***, not to the detection of ***physical molecular modifications to a molecule of interest***, as is defined by the claimed invention. The Office Action admits as much. For example, page 6 of the Office Action states that "Kask discloses homogenous drug screening methods using fluorescently labeled samples for identifying ligands (e.g. calmodulin), whose fluorescence lifetime is influence by ***protein-peptide*** interaction." (emphasis added). Kask also makes this distinction clear. For example, Kask teaches various examples of fluorescently-labeled proteins in "Experiment 1" at paragraphs 0080-0084, including fluorescently-labeled calmodulin, and the detection or characterization of their interprotein binding events.

The present invention, on the other hand, is directed to methods for detecting physical modifications or changes that occur directly to a molecule of interest which are the result of the action of a modifying agent that converts the molecule from one physical state to another. In other words, the inventive method detects changes in the physical state or structure of a molecule of interest, rather than a method that detects a protein-protein binding interaction or event, as disclosed by Kask.

Accordingly, Kask does not meet all of the claim limitations. In particular, Kask does not teach or suggest a method of detecting a ***modification to a molecule*** that involves (a) ***measuring*** the fluorescence lifetime of the fluorescently labeled molecule when it is in a first state; (b) ***contacting*** the molecule with a modifying agent that is capable of changing the molecule from said first state to a second state; and (c) ***measuring*** the fluorescence lifetime of the fluorescently labeled molecule after contacting with the modifying agent, wherein a difference in the fluorescence lifetimes measured in (a) and (c) indicates a modification to the molecule. In addition, Kask does not teach or disclose a method of screening for a ***modifying agent that is capable of modifying a molecule in a first state to a molecule in a second state***, wherein the molecule is fluorescently labeled and has a different fluorescent lifetime in a first state as compared to a second state, comprising (a) ***measuring*** the fluorescence lifetime of the fluorescently-labeled molecule in the first state, (b) ***contacting*** the fluorescently-labeled molecule in the first state with a candidate modifying agent, (c) ***measuring*** the fluorescence lifetime of the fluorescently-labeled molecule after it has been contaced with the candidate

modifying agent, and (d) ***comparing*** the fluorescence lifetimes measured in step (a) and step (c), wherein the candidate modifying agent is identified as a modifying agent where there exists a difference in the fluorescent lifetimes.

Moreover, Kask's methods are plainly different than those of the present invention. While the methods of the present invention are directed to fluorescence lifetime measurements of fluorescently-labeled molecules that are physically changed from one state to another by some modification, Kask teaches a "two-dimensional" analysis that involves measuring both "specific brightness" as well as "lifetime values" and "concentration" in the context of protein-protein binding interactions. See paragraph 0011 of Kask. Specifically, Kask teaches that "a method has been developed that is suited to discriminate different species of a sample according to their lifetimes, τ, and brightness values, q, as well as to detemine their absolute concentrations, c." See paragraph 0012 of Kask. The present invention does not require any steps involving the determining of specific brightness or concentrations of the fluorescently-labeled molecules of interest. Thus, Kask's methods are different and distinguishable from the methods of the present invention.

Because Kask does not meet all the claim limitations of the instant claims, the present invention as defined in claims 10-29 is not anticipated. Accordingly, in view of at least the above, Applicants respectfully request reconsideration and withdrawal of the Section 102 rejection.

5. The Rejection Under 35 U.S.C. 103 Is Overcome

The Examiner rejected claim 8 under 35 U.S.C. 103(a) as allegedly being obvious over Kask in view of Giuliano et al. (U.S. Patent No. 6,416,959) (hereafter as "Giuliano"). Claim 8 has been cancelled, without prejudice, thereby rendering the rejection moot. Presently, no claim is presented with corresponds to the limitations of claim 8. Accordingly, Applicants respectfully request reconsideration and withdrawal of the obviousness rejection.

CONCLUSION

In view of the remarks herein, Applicants respectfully request reconsideration and withdrawal of all of the rejections as Applicants believe the application to be in condition for allowance. Favorable reconsideration of the application and prompt issuance of a Notice of Allowance are respectfully requested. Please charge any required fee or credit any overpayment to Deposit Account No. 04-1105 under reference number 84376(303989).

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Respectfully submitted,

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